PROFILES, PATHWAYS, AND DREAMS

Autobiographies of Eminent Chemists

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Steroids Made It Possible

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Applications of Computer Artificial Intelligence Techniques

During Stanford University's initial courting of me in early 1959, three faculty members, aside from the legendary provost F. E. Terman, spent much time with me: Joshua Lederberg, then chairman of the Genetics

Opening of the Syntex Institute of Molecular Biology in the Stanford Industrial Park, circa 1962. Left to right: Carl Djerassi, Charles Allen, Jr. (investment banker from Allen & Company, New York, NY), and Joshua Lederberg.

Department and since 1978 president of Rockefeller University; Arthur Kornberg, chairman of the Biochemistry Department; and the late Henry Kaplan, then chairman of the Radiology Department. All three became personal friends, but the longest and professionally most intimate relationship was with Joshua Lederberg. After I had accepted the Stanford offer in 1959, but while I was still living in Mexico City and commuting periodically to the Bay area, Lederberg and his wife visited us in Mexico. They even introduced us to the architect who built our California home in time for our September 1960 arrival.

Within 2 years, Lederberg was serving as principal scientific advisor of the Syntex Institute for Molecular Biology, which I had induced my fellow Syntex directors to establish on the Stanford Industrial Park and for which I took overall responsibility. I had felt that Syntex should diversify beyond steroids, and molecular biology seemed an ideal vehicle: It promised exciting new science, potential medical applications, and, most importantly, the presence of several academic pioneers on the Stanford faculty. The Syntex Institute, though small, was probably the earliest American industrial laboratory dedicated specifically to exploring practical applications of the burgeoning field of molecular biology.

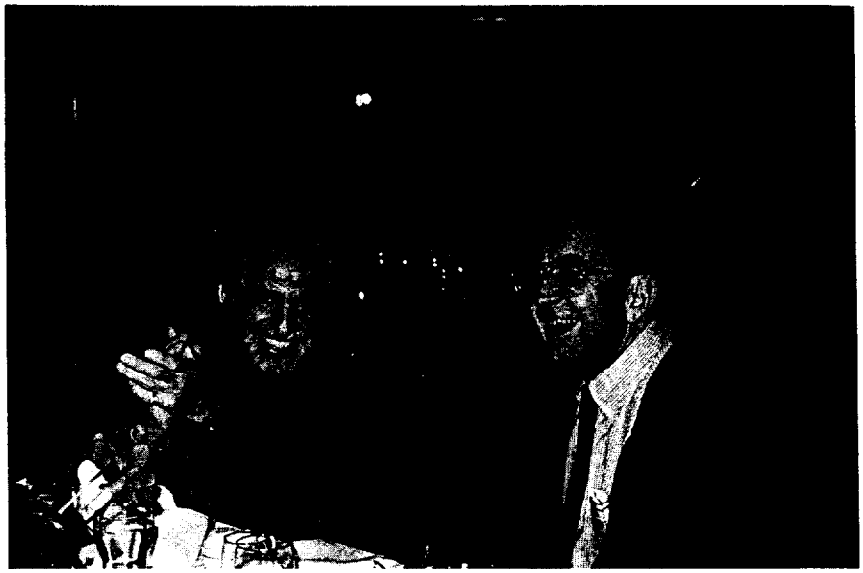
Fred Terman, Stanford's provost and virtual founder of the Industrial Park, was delighted that a chemically and biomedically oriented corporation was prepared to join what, until then, was a group of corporations exclusively dedicated to electronics, computers, and publishing. Within a year, I persuaded my fellow board members to establish Syntex's United States operations in Palo Alto. By the middle 1960s most of Syntex's research had also moved from Mexico City to Palo Alto to join the Molecular Biology Institute, which was the beginning of the company's research efforts outside the area of steroid chemistry and medicine. Twenty years later, Syntex, by now a billion-dollar company, has become the largest occupant of the Stanford Industrial Park and has spawned several other research-oriented companies such as ALZA, SYVA, and Zoecon. The middle 1960s was also the period when my polygamous professional life really flourished. When my close friend and colleague, Alejandro Zaffaroni, left his position as president of Syntex Research to found ALZA and pursue his interest in novel drug delivery methods, I succeeded him as president without giving up my Stanford academic position. At the same time, I helped found (and served as board chairman of) SYVA—a joint venture of Syntex and Varian—which became one of the truly innovative companies in the medical diagnostic field. Zoecon, which was created in 1968 to concentrate on novel approaches to insect control, became my real industrial baby. In 1972, I discontinued my connection with Syntex, and thereafter focused the industrial portion of my bigamous life on Zoecon as its CEO until it was acquired in 1983 by the Swiss pharmaceutical company Sandoz.

Aside from our social interaction, I saw Lederberg professionally several times per week, usually at lunch. Until today, I have never met anybody with such a quick mind and such broad interests. There was no topic—not even esoteric chemical ones—that could not be discussed with him and that would not be countered with insightful comments. It was not surprising, therefore, that Lederberg became quite familiar with our flourishing mass spectrometric research during a period when he, the Nobel-Prize-winning bacterial geneticist, had become deeply interested in exobiology.

Lederberg was one of America's chief proponents of unmanned flights to outer space and had established, with the assistance of Elliot Levinthal (who also became a good friend), a sophisticated instrumenta-

One of the most enjoyable events during my Zoecon career was the visit of King Carl XVI Gustaf of Sweden with a group of Swedish industrialists. Here he is looking amusedly at some cockroaches held by Gerardus Staal (director of insect research at Zoecon). Between the king and me is Karl-Erik Sahlberg (president of Perstorp AB), and at the right is Bengt Modeer of the Swedish Academy of Engineering Sciences.

tion laboratory for the development of devices that might detect evidence of life in the forthcoming lunar and Mars missions. Mass spectrometry was high on his list of instrumental priorities and, because he was focusing on unmanned flights, computer control of the various instruments and experiments was crucial. Lederberg's interest in automated instrumentation for exobiology led him to apply topological graph theory to the classification of organic molecules, the forerunner of DENDRAL[206] (acronym for dendritic algorithm). He subsequently collaborated with Edward Feigenbaum on the implementation of DENDRAL, in what came to be known as knowledge-based systems of artificial intelligence. Feigenbaum was one of the founders of the field of computer artificial intelligence and subsequently became the chairman of Stanford's Department of Computer Science. Their collaboration lasted for over 15 years and, with many research fellows and students, produced the famous DENDRAL system,[207] which formed the basis of the computer-aided structure elucidation approaches in which I participated.



With Ed Feigenbaum at his 50th birthday party in 1986.

Applications in Mass Spectrometry

Lederberg's involvement in mass spectrometry started in 1963, when he developed a very convenient algorithm for calculating molecular formulas from high-resolution mass spectral data. With the advent of high-resolution mass spectrometers and penetration of ever-higher mass ranges, questions such as "given a molecular ion peak of 718.3743 ± .0060, what empirical formulas are consistent with such a value?" are hardly trivial. Lederberg's clever and convenient solution was published in abbreviated form as an appendix to one of our books[125] and subsequently in an independent volume.

Insofar as mass spectrometry was concerned, Lederberg's exobiology problem could be stated in simple terms: What is the maximum structural information that can be extracted from a mass spectrum measured on Mars and returned to earth by telemetry? In this context, Lederberg and Feigenbaum invited me in 1967 to join their DENDRAL project as the chemical member of a triumvirate that would focus on "Applications of Artificial Intelligence for Chemical Inference." This became the fourth new research area undertaken by my research group at Stanford and also the lead title in a series of publications that culminated in my 1982 IUPAC lecture, "Computational Aids to Natural Products Structure Elucidation."[208]